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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/623,076	01/12/2001	Miles Douglas Houslay	9013-19	7015

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EXAMINER	
SHEINBERG, MONIKA B	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 09/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/623,076	HOUSLAY ET AL.
	Examiner	Art Unit
	Monika B Sheinberg	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *11-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-18* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *1sheet* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-10, drawn to a method of sequence determination.

Group II, claims 11-18, drawn to a computer program.

Group III, claim 13, drawn to a sequencing apparatus.

Group IV, claims 14-18, drawn to a kit.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Claim 1 is anticipated by Brenner *et al.* (*PNAS,* 1989; *PTO-1449*). Brenner *et al.* demonstrates a method that comprises cleaving the polynucleotide with type IIs restriction enzymes to create 5' overhangs followed by filling in the recessed ends with a polymerase to create blunt ends for the end result of determining a nucleic acid sequence by cloning and sequencing for the basis of "mak[ing] a reliable assignment of overlaps between clones" (p. 8902, 1st column, 1st paragraph, lines 6-16). As such the listed Groups I-IV do not relate to a single general inventive concept.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Election

During a telephone conversation with Michael Sajovec on 27 April 2003 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-10. Affirmation of this election must be made by applicant in replying to this Office action.

Claims 11-18 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-10 have been examined.

Sequence Non-Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825 because there are nucleic acid sequences within the specification that do not have a sequence identifiers: see page 21, last line; page 22, 1st line, and Figure 2 of the Drawings. A Sequence Listing and a computer readable format of it must be provided with a statement that the two are identical. The sequence presented in the specification and figure must still be included in the Sequence Listing; and a sequence identifier (SEQ ID NO: X) must be used, either in the drawing or in the Brief Description of the Drawings in regards to the figure, and within the specification in regards to pages 21 and 22. Applicant is reminded that CD-ROM sequence listings are now accepted instead of a paper copy of the sequence listing for the specification. Applicant(s) are given the same response time regarding this failure to comply as that set forth to respond to this office action. *A complete response to this office action includes compliance with this sequence rule compliance. Failure to comply may result in abandonment of this application.*

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Great Britain 9803930.8; on February 26, 1998. It is noted, however, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

- Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite due to the lack of clarity of the term "reading" (step e). The metes and bounds of the parameters that describe reading are unclear; i.e. is it a mental step? As such claims 2-10 are also indefinite due dependency from claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- Claims 1-5 and 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Brenner *et al.* (*PNAS,* 1989; *PTO-1449*).

Brenner et al demonstrates a sequence characteriztion method that comprises cleaving the polynucleotide with type IIS restriction enzymes to create 5' overhangs followed by filling in the recessed ends with a DNA polymerase to create blunt ends [claim 1 (a-b), p. 8904, 1st column, 2-3rd paragraph] for the end result of determining a nucleic acid sequence by cloning and automated sequencing using the Genesis 2000 DNA analysis system [claims 1 (d-e), 9 and 10; abstract and p. 8904, 2nd column, 1-2nd paragraph]. The ambiguous overhangs which are filled in by dNTPs (claim 5) are thus utilized for the basis of "mak[ing] a reliable assignment of overlaps between clones" (claim 8, p. 8902, 1st column, 1st paragraph, lines 6-16). Page 8904 (1st column, 3rd paragraph, lines 10-18) describes the use of any enzymes for the primary cleavage and *FokI* for the secondary cleavage as required by claim 4. The use of *FokI* (claim 3) results in a greater than 3 base pair overhang as required by claim 2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

- Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner *et al.* (*PNAS*, 1989; *PTO-1449*) in view of Marchuk *et al.* (*Nuc. Acids Res.*, 1990).

Brenner et al demonstrates a sequence characteriztion method that comprises cleaving the polynucleotide with type IIS restriction enzymes to create 5' overhangs followed by filling in the recessed ends with a DNA polymerase to create blunt ends [claim 1 (a-b), p. 8904, 1st column, 2-3rd paragraph] for the end result of determining a nucleic acid sequence by cloning and automated sequencing using the Genesis 2000 DNA analysis system [claims 1 (d-e), 9 and 10; abstract and p. 8904, 2nd column, 1-2nd paragraph]. The ambiguous overhangs which are filled in by dNTPs (claim 5) are thus utilized for the basis of "mak[ing] a reliable assignment of overlaps between clones" (claim 8, p. 8902, 1st column, 1st paragraph, lines 6-16). Page 8904 (1st column, 3rd paragraph, lines 10-18) describes the use of any enzymes for the primary cleavage and *FokI* for the secondary cleavage as required by claim 4. The use of *FokI* (claim 3) results in a greater than 3 base pair overhang as required by claim 2.

Brenner *et al.* does not teach the limitations of claim 7 wherein "the blunt-ended fragments posses a single adenine 3'-overhang and te cloning of said fragments is facilitated

using a cleaved vector comprising single thymidine 5'-ohverhangs at the cleavage site" (lines 2-4); nor the use of a specific polymerase as listed in claim 6.

Marchuk *et al.* demonstrates an efficient method of cloning by the construction of T-vectors. In the event that restriction enzymes are used for overhang cuts, blunt ended fragments of the digested nucleic acids "can be made by filling in using the Klenow (5'overhang)" fragment of DNA polymerase I, as required by claim 6. Once as blunt ended fragments, they are "subsequently treated with Taq polymerase in the presence of dATP" (p. 1154, 2nd column, last paragraph) wherein a single adenine 3'overhang are created on blunt-end fragments to be cloned for facilitating cloning into thymidine 5' overhang cleaved vectors.

It would have been *prima facia* obvious for one of ordinary skill in the art at the time the invention was made to have performed the sequence characterization method of Brenner *et al.* and further modify the method to include the improved cloning technique of the TA-cloning method as per the teachings of Marchuk *et al.* Thus, one of ordinary skill in the art would have been motivated to do the modifications taught by Marchuk *et al.* due to the advantages of observed high efficiency (2nd column, 1st paragraph) with in a "simple procedure [...that] can be readily adapted to any plasmid or viral DNA based vector with a unique bluht ended restriction endonuclease site"(2nd column, last paragraph). In addition common problems of general cloning procedures are eliminated, "[v]ector self-ligation events are prohibited by the 3' thymidine overhang, and concatamerization of the insert is prohibited by the unphosphorylated 5' end" (2nd column, last paragraph). Thus it would have been *prima facia* obvious for one of ordinary skill in the art at the time the invention was made to have performed the sequence characterization method of Brenner *et al.* in view of Marchuk *et al.*

Specification Objection

The disclosure is objected to because of the following informalities: content of the specification does not follow the appropriate MPEP requirements. (See insert below). Appropriate correction is required.

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data

shet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

Or alternatively, Reference to a "Microfiche Appendix": See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.

(e) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(h) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet (37 CFR 1.52(b)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(j) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an

international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(k) Sequence Listing. See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

Conclusion

- Sequence Non-Compliance.
- Priority: No certified copy of the foreign reference has been provided.
- Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph.
- Claims 1-5 and 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Brenner *et al.*
- Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brenner *et al.* in view of Marchuk *et al.*
- Objection to the specification.

No claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 9 A.M to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the primary examiner in charge of the prosecution of this case, Jehanne Souaya, can be reached at 703-308-6565. If attempts to reach the examiners are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (703) 605-1237, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

September 8, 2003
Monika B. Sheinberg
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